REMARKS

In the Office Action dated December 14, 2009, Claims 1, 3, 5-10 and 13-29 were pending in the application, of which claims 13-29 were withdrawn from further consideration as drawn to non-elected inventions. Claims 1, 3 and 5-10 were considered and were rejected under 35 U.S.C. §103(a), as allegedly unpatentable over Morin et al. (*Clinical & Experimental Immunology* 134(3): 388-395, 2003) ("Morin" hereinafter).

This Response addresses the Examiner's rejection. Applicants therefore respectfully submit that the present application is in condition for allowance. Favorable consideration of all pending claims is therefore respectfully requested.

Claim Amendments

Claim 1, the only independent claim, has been amended to specify that "Flt-3L is administered to said subject as the sole active component". Support for this feature is found in the specification, e.g., on page 10, lines 13-15 (referring to administering Flt-3L "alone or in combination with other molecules"). Further, in the example section on page 33 (Example 2) and pages 42-44 (Examples 10-12) of the specification, the beneficial effects were shown with administration of Flt-3L *alone*, free of other active agents such as cytokines.

Claims 3 and 5-6 have been canceled in light of the amendments to claim 1.

Claim 30 is added, which delineates the subject as "pre-disposed to developing diabetes", as supported by the disclosure on page 10, lines 3-6, for example.

No new matter is introduced by the foregoing amendments. Entry thereof is respectfully requested.

35 U.S.C. §103(a)

According to the Examiner, Morin teaches transplantation of *in vivo* Flt-3L cultured-dendritic cells into non-obese diabetic (NOD) mice delays diabetes development in these recipient NOD mice. Furthermore, Morin is noted to state that "[w]e hypothesize that flt-3L-DC represent the *in vitro* counterparts of a subset, or a maturational state, of DC that is defective in NOD mice and cannot be derived easily from BM progenitors cultured with GM-CSF + IL-4....Specific stimulation of this subset of DC may open new possibilities of therapeutic intervention to prevent diabetes onset." Therefore, the Examiner contends that Morin conceived of the idea of stimulating dendritic cells *in vivo* with Flt-3L to increase a sub-type of non-activated, immature and tolerogenic DC in order to delay the onset of diabetes.

The Examiner further reasons that, while Morin does not specifically state what this "therapeutic intervention" might be, one skilled artisan could quickly conceive of two possibilities from the cited art: (1) transplantation of Flt-3L stimulated dendritic cells or (2) administration of recombinant Flt-3L. Therefore, it is the Examiner's position that while Morin does not explicitly teach the claimed method where Flt-3L is administered to a subject to delay onset of diabetes, the disclosure of Morin suggests such method.

Thus, the Examiner concludes that those skilled in the art would have been motivated to administer Flt-3L to a subject to delay onset of diabetes, and would have expected success because Flt-3L has been shown to mature a population of dendritic cells such that these cells are capable of delaying onset of diabetes in a diabetic mouse model.

Applicants respectfully disagree.

First, the Examiner has referenced several times "*in vivo* flt-3L-cultured DC" in Morin. Applicants note that the so-called "flt-3L-DC" of Morin were derived from cells cultured *in vitro*.

Further, the experimental data presented in Morin show that Morin produced these flt-3L-DC by stimulation of spleen cells cultured *in vitro* with a mix of three cytokines, namely GM-CSF + Flt-3L + IL-6. See abstract and page 388, column 2, last paragraph of Morin. This is in contrast to the claimed invention which involves administration of Flt-3L as the sole active agent. Morin does not disclose stimulation with Flt-3L alone, either *in vitro* or *in vivo*, to derive a desirable subset of DC.

Moreover, Morin's DC, which were produced *in vitro* by culture in the presence of three cytokines are CD11b+ve/CD8-ve/MHCII+ve and are myeloid-related mature DC. See Morin, page 390, column 2 to page 391, column 1 through to line 7, and page 394, column 1, 2nd paragraph, lines 15-16 & last paragraph, 2nd sentence. These CD8-ve DC are different from the DC increased in number by the present invention. More specifically, in accordance with the present invention, administration of Flt-3L *in vivo* alone results in an increased number of sub-types of immature DC which are CD8+ve and plasmacytoid DC. It was the increase in numbers of these DC in response to administration of Flt-3L alone that results in delay of the onset of diabetes. See Figure 1, Table 2 and Examples 10-15 of the present application.

For these reasons, Applicants respectfully submit that the Examiner is misguided in stating that "Morin conceived of the idea of stimulating dendritic cells *in vivo* with Flt-3L to increase a sub-type of non-activated, immature and tolerogenic DC in order to delay the onset of diabetes." Morin simply does not disclose stimulating dendritic cells *in vivo*, or stimulating cells with Flt-3L alone *in vivo* or *in vitro*, and Morin's stimulation approach results in different cells.

Further, Applicants respectfully submit that the Examiner is misguided in stating that Morin suggests Flt-3L administration as a therapeutic intervention. In fact, Morin suggests that specific stimulation of "this subset of DC" (see page 394, column 1, last paragraph) may open possibilities of therapeutic intervention. That is, Morin is referring to the DC produced *in vitro* from a culture with a mix of three cytokines. Moreover, there is nothing in Morin suggesting that this particular set of DC of Morin could even be reproduced or expanded by *in vivo* stimulation. Therefore, those skilled in the art would not have considered Morin's teaching, which is directed to limited *in vitro* culture conditions with a mix of three cytokines to represent any suggestion or reasonable expectation of success, to stimulate with Flt-3L alone *in vivo* to delay the onset of diabetes.

Accordingly, Applicants respectfully submit that the method as presently claimed is not obvious over Morin. Withdrawal of the rejection under 35 U.S.C. §103(a) is respectfully requested.

Conclusion

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

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